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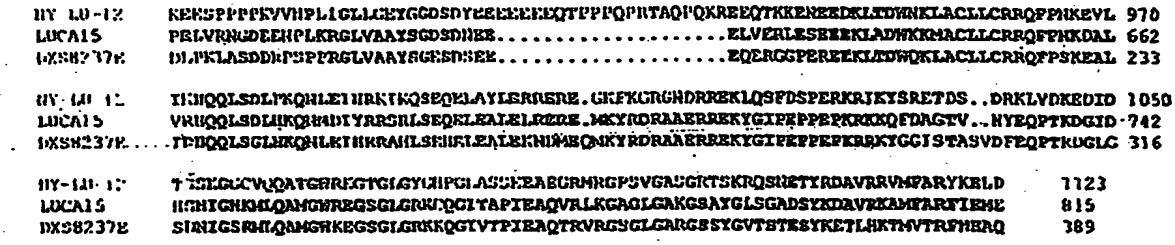
(54) Title: CANCER ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES



(57) Abstract

Various molecules associated with cancer are disclosed. The invention also discloses diagnostic and therapeutic methods based upon these molecules.

the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code.

The invention also provides isolated unique fragments of cancer associated antigen nucleic acid sequences or complements thereof. A unique fragment is one that is a 'signature' for the larger nucleic acid. It, for example, is long enough to assure that its precise sequence is not found in molecules within the human genome outside of the cancer associated antigen nucleic acids defined above (and human alleles). Those of ordinary skill in the art may apply no more than routine procedures to determine if a fragment is unique within the human genome. Unique fragments, however, exclude fragments completely composed of the nucleotide sequences of any of GenBank accession numbers listed in Table 1 or other previously published sequences as of the filing date of the priority documents for sequences listed in a respective priority document or the filing date of this application for sequences listed for the first time in this application which overlap the sequences of the invention.

A fragment which is completely composed of the sequence described in the foregoing GenBank deposits is one which does not include any of the nucleotides unique to the sequences of the invention. Thus, a unique fragment must contain a nucleotide sequence other than the exact sequence of those in GenBank or fragments thereof. The difference may be an addition, deletion or substitution with respect to the GenBank sequence or it may be a sequence wholly separate from the GenBank sequence.

Unique fragments can be used as probes in Southern and Northern blot assays to identify such nucleic acids, or can be used in amplification assays such as those employing PCR. As known to those skilled in the art, large probes such as 200, 250, 300 or more nucleotides are preferred for certain uses such as Southern and Northern blots, while smaller fragments will be preferred for uses such as PCR. Unique fragments also can be used to produce fusion proteins for generating antibodies or determining binding of the polypeptide fragments, or for generating immunoassay components. Likewise, unique fragments can be employed to produce nonfused fragments of the cancer associated antigen polypeptides, useful, for example, in the preparation of antibodies, and in immunoassays. Unique fragments further can be used as antisense molecules to inhibit the expression of cancer associated antigen nucleic acids and polypeptides, particularly for therapeutic purposes as described in greater detail below.

human cytomegalovirus (CMV) enhancer-promoter sequences. Additionally, suitable for expression in primate or canine cell lines is the pCEP4 vector (Invitrogen), which contains an Epstein Barr Virus (EBV) origin of replication, facilitating the maintenance of plasmid as a multicopy extrachromosomal element. Another expression vector is the pEF-BOS plasmid containing the promoter of polypeptide Elongation Factor 1α, which stimulates efficiently transcription *in vitro*. The plasmid is described by Mishizuma and Nagata (*Nuc. Acids Res.* 18:5322, 1990), and its use in transfection experiments is disclosed by, for example, Demoulin (*Mol. Cell. Biol.* 16:4710-4716, 1996). Still another preferred expression vector is an adenovirus, described by Stratford-Perricaudet, which is defective for E1 and E3 proteins (*J. Clin. Invest.* 90:626-630, 1992). The use of the adenovirus as an Adeno.P1A recombinant for the expression of an antigen is disclosed by Warnier et al., in intradermal injection in mice for immunization against P1A (*Int. J. Cancer*, 67:303-310, 1996). Additional vectors for delivery of nucleic acid are provided below.

The invention also embraces so-called expression kits, which allow the artisan to prepare a desired expression vector or vectors. Such expression kits include at least separate portions of a vector and one or more of the previously discussed breast cancer associated antigen nucleic acid molecules. Other components may be added, as desired, as long as the previously mentioned nucleic acid molecules, which are required, are included. The invention also includes kits for amplification of a breast cancer associated antigen nucleic acid, including at least one pair of amplification primers which hybridize to a breast cancer associated antigen nucleic acid. The primers preferably are 12-32 nucleotides in length and are non-overlapping to prevent formation of "primer-dimers". One of the primers will hybridize to one strand of the breast cancer associated antigen nucleic acid and the second primer will hybridize to the complementary strand of the breast cancer associated antigen nucleic acid, in an arrangement which permits amplification of the breast cancer associated antigen nucleic acid. Selection of appropriate primer pairs is standard in the art. For example, the selection can be made with assistance of a computer program designed for such a purpose, optionally followed by testing the primers for amplification specificity and efficiency.

The invention also permits the construction of cancer associated antigen gene "knock-outs" in cells and in animals, providing materials for studying certain aspects of cancer and immune system responses to cancer.

The invention also provides isolated polypeptides (including whole proteins and partial

ID AAX39745 standard; DNA; 780 BP.
XX
AC AAX39745;
XX
DT 02-JUL-1999 (first entry)
XX
DE Gastric cancer associated gene.
XX
KW Cancer associated antigen; diagnosis; research; treatment; human;
KW breast cancer; colon cancer; gastric cancer; renal cancer; lung cancer;
KW prostate cancer; ss.
XX
OS Homo sapiens.
XX
PN WO9904265-A2.
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PD 28-JAN-1999.
XX
PF 15-JUL-1998; 98WO-US14679.
XX
PR 22-JUN-1998; 98US-0102322.
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PR 10-OCT-1997; 97US-0948705.
PR 11-OCT-1997; 97GB-0021697.
XX
PA (LUDW-) LUDWIG INST CANCER RES.
XX
PI Chen Y, Gout I, Gure A, O'Hare M, Obata Y, Old LJ;
PI Pfreundschuh M, Sahin U, Scanlan MJ, Stockert E;
PI Tureci O;
XX
DR WPI; 1999-132448/11.
XX
PT New isolated cancer associated nucleic acids and polypeptides -
PT isolated using sera from cancer patients, used to develop products
PT for the diagnosis, monitoring or treatment of cancers
XX
PS Claim 67; Page 532; 787pp; English.
XX
CC The invention relates to a method for diagnosing a disorder characterised
CC by expression of a human cancer associated antigen precursor coded for by
CC a nucleic acid molecule (NAM). The method comprises: (a) contacting a
CC biological sample isolated from a subject with an agent that specifically
CC binds to the NAM, an expression product or a fragment of an expression
CC product complexed with an HLA molecule; and (b) determining the
CC interaction between the agent and the NAM or the expression product as a
CC determination of the disorder. The products and methods can be used in
CC the diagnosis, monitoring, research, or treatment of conditions
CC characterised by the expression of various cancer associated antigens.
CC The invention provides nucleic acid sequences and encoded polypeptides
CC which are cancer associated antigen precursors expressed in human breast
CC cancer, renal cancer, colon cancer, gastric cancer, prostate cancer and
CC lung cancer.
XX
SQ Sequence 780 BP; 303 A; 140 C; 182 G; 150 T; 5 other;

attctgaggg tatattaagt cagagtcagg ataaatcact tcggagaata gcagaattaa 60
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